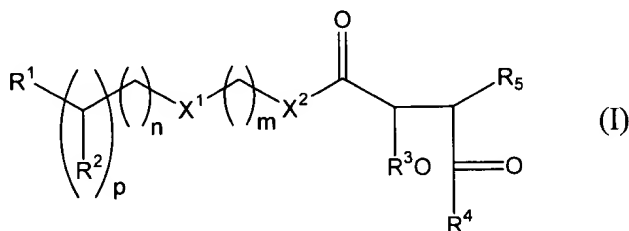


a.) Amendments to the Claims

1. (Currently Amended) A method to inhibit proteasome ~~inhibitor~~ comprising, ~~as an active ingredient,~~ a step of administering to a mammal an effective amount of a ~~carboxylic acid derivative~~ a compound represented by the formula (I) or a pharmaceutically acceptable salt thereof:



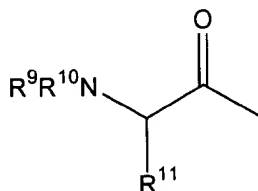
~~wherein~~ wherein

m and n ~~are the same or different and~~ independently represent an integer of 0 to 10;

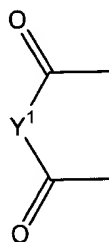
p represents 0 or 1;

R¹ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alicyclic alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or NR⁶R⁷ {wherein R⁶ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl, and R⁷ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW¹R⁸ (wherein R⁸ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkylamino, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted aralkyl,

substituted or unsubstituted aralkylamino, or substituted or unsubstituted aralkyloxy, and W¹ represents an oxygen atom or a sulfur atom), or the formula:



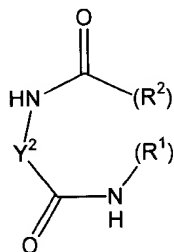
(wherein R⁹ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl; R¹⁰ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW²R^{8a} (wherein R^{8a} and W² have the same significance meanings as ~~the above~~ R⁸ and W¹, respectively), substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, or PW³R¹²₂ (wherein R¹²'s ~~are the same or different and~~ independently represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and W³ has the same significance meaning as ~~the above~~ W¹); or R⁹ and R¹⁰ together represent the formula:



(wherein Y¹ represents substituted or unsubstituted alkylene or substituted or unsubstituted arylene); and R¹¹ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl));

R² represents a hydrogen atom, COR¹³ (~~wherein~~ wherein R¹³ represents hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted

alkenyloxy, substituted or unsubstituted aralkyloxy, substituted or unsubstituted alicyclic alkylalkoxy, substituted or unsubstituted aroylalkoxy, or $\text{NR}^{14}\text{R}^{15}$ (wherein R^{14} represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and R^{15} represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkoxycarbonylalkyl, amino, substituted or unsubstituted alkylamino, or substituted or unsubstituted arylamino; or R^{14} and R^{15} together with the adjacent N form a substituted or unsubstituted heterocyclic group)) or $\text{CH}_2\text{OR}^{3a}$ (wherein group))} or $\text{CH}_2\text{OR}^{3a}$ {wherein R^{3a} represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aroyl, or SiR^{16}_3 (wherein R^{16} 's are the same or different and independently represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl)); aryl)} or R^1 and R^2 together represent the formula:



(wherein Y^2 represents substituted or unsubstituted alkylene);

X^1 represents a bond, substituted or unsubstituted alkylene, substituted or unsubstituted alicyclic alkylene, substituted or unsubstituted alkenylene, or substituted or unsubstituted arylene;

X^2 represents an oxygen atom, a sulfur atom or NR^{17} (wherein R^{11} represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl);

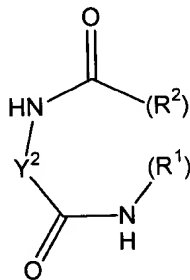
R^3 has the same ~~significance~~ meaning as ~~the above~~ R^{3a} ;

R^4 represents hydroxy, mercapto, substituted or unsubstituted alkoxy, or substituted or unsubstituted alkylthio; or R^3 and R^4 together represent a bond; and

R^5 represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted ~~aralkyl~~ aralkyl.

2. (Currently Amended) The method to inhibit proteasome ~~inhibitor~~ according to claim 1, wherein R^3 and R^4 together represent a bond.

3. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 1, wherein R^4 is hydroxy, or substituted or unsubstituted alkoxy; p is 1; R^1 is a hydrogen atom or NR^6 R^7 (~~wherein each of R^6 and R^7 has the same significance as defined above~~), or R^1 and R^2 together ~~are the formula~~ form:



(wherein Y^2 has the same significance as defined above); X^1 is substituted or unsubstituted alicyclic alkylene, or substituted or unsubstituted arylene; and X^2 is NR^{17} (wherein R^{17} has the same significance as defined above).

4. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 1, wherein R^4 is mercapto, or substituted or unsubstituted alkylthio, or R^3 and R^4 together are a bond; X^2 is NR^{17} (wherein R^{17} has the same significance as defined above) [when with the proviso that when m is 0; n and p are 1; R^2 is carboxy; R^3 and R^4 together are a bond; R^5 is sec-butyl; and X^1 is cyclopropylene or ethylene, then R^1 is neither $NHC(=O)-C(CH_3)NH_2$ nor $NHC(=O)-C(CH_3)NHC(=O)O-C(CH_3)_3$].

5. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 3, wherein R^1 is a hydrogen atom or NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above).

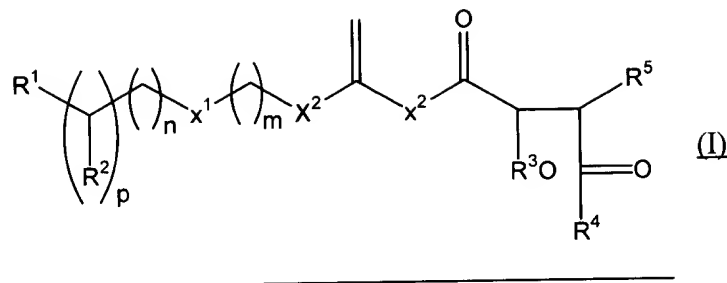
6. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 5, wherein R^1 is NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above); X^1 is cyclopropylene or alkylene; and X^2 is NH.

7. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 4, wherein R⁴ is mercapto, or substituted or unsubstituted alkylthio; R¹ is NR⁶R⁷ (~~wherein each of R⁶ and R⁷ has the same significance as defined above~~); and X¹ is cyclopropylene or alkylene.

8. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 4, wherein R³ and R⁴ together are a bond.

9. (Currently Amended) The ~~carboxylic acid derivative or the pharmaceutically acceptable salt thereof~~ method to inhibit proteasome according to claim 8, wherein m is 0; n and p are 1; R¹ is NR⁶R⁷ (~~wherein each of R⁶ and R⁷ has the same significance as defined above~~); R² is COR^{13a} (wherein R^{13a} is alkylamino, aralkyloxy or aralkylamino); R⁵ is alkyl; X¹ is cyclopropylene, alkylene, or substituted or unsubstituted phenylene; and X² is NH.

10. (Currently Amended) A process for producing ~~the carboxylic acid derivative according to claim 1~~ a compound represented by the formula (I) or a pharmaceutically acceptable salt thereof



wherein

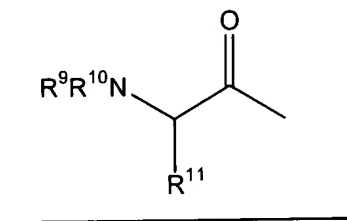
m and n independently represent an integer of 0 to 10;

p represents 0 or 1;

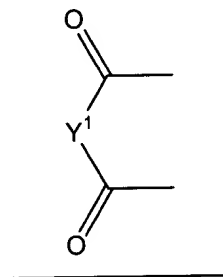
R¹ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alicyclic alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or NR⁶R⁷ {wherein R⁶ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl, and R⁷ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW¹R⁸ (wherein R⁸ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkylamino, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted aralkyl,

substituted or unsubstituted aralkylamino, or substituted or unsubstituted aralkyloxy, and

W¹ represents an oxygen atom or a sulfur atom), or the formula:



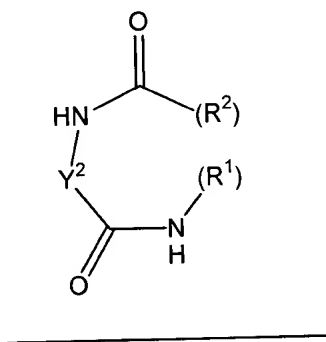
(wherein R⁹ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl; R¹⁰ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW²R^{8a} (wherein R^{8a} and W² have the same meanings as R⁸ and W¹, respectively), substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, or PW³R¹²₂ (wherein R¹²'s independently represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and W³ has the same meaning as W¹); or R⁹ and R¹⁰ together represent the formula:



(wherein Y¹ represents substituted or unsubstituted alkylene or substituted or unsubstituted arylene); and R¹¹ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl)};

R² represents a hydrogen atom, COR¹³ {wherein R¹³ represents hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyloxy,

substituted or unsubstituted aralkyloxy, substituted or unsubstituted alicyclic alkylalkoxy, substituted or unsubstituted aroylalkoxy, or $\text{NR}^{14}\text{R}^{15}$ (wherein R^{14} represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and R^{15} represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkoxycarbonylalkyl, amino, substituted or unsubstituted alkylamino, or substituted or unsubstituted arylamino; or R^{14} and R^{15} together with the adjacent N form a substituted or unsubstituted heterocyclic group)) or $\text{CH}_2\text{OR}^{3a}$ {wherein R^{3a} represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aroyl, or SiR^{16}_3 (wherein R^{16} 's independently represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl)}, or R^1 and R^2 together represent the formula:



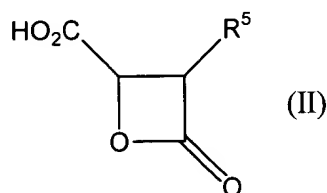
(wherein Y^2 represents substituted or unsubstituted alkylene):

X^1 represents a bond, substituted or unsubstituted alkylene, substituted or unsubstituted alicyclic alkylene, substituted or unsubstituted alkenylene, or substituted or unsubstituted arylene; and

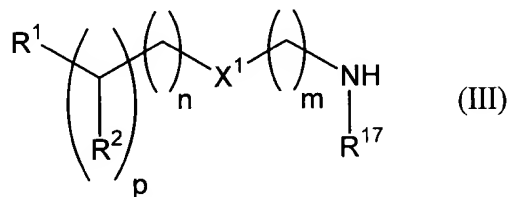
X^2 is NR^{17} (wherein R^{17} represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl):

R⁵ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted aralkyl, characterized in that comprising the steps of:

reacting a carboxylic acid represented by the formula (II):



~~(wherein R⁵ has the same significance as defined above)~~ is reacted with an amine represented by the formula (III):

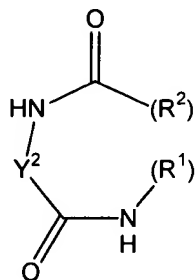


~~(wherein each of m, n, p, R¹, R², R¹⁷ and X¹ has the same significance as defined above).~~

11. (Currently Amended) The ~~carboxylic acid~~ process according to claim 10, wherein R⁵ is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted aralkyl, or a salt thereof.

12. (Currently Amended) The process ~~amine~~ according to claim 10, wherein m is 0; n and p are 1; R¹ is NR⁶R⁷ ~~(wherein each of R⁶ and R⁷ has the same significance as defined above);~~ R² is COR¹³ ~~(wherein R¹³ has the same significance as~~

~~defined above~~) or $\text{CH}_2\text{OR}^{3a}$ (~~wherein R^{3a} has the same significance as defined above~~), or R^1 and R^2 together are the formula:



~~(wherein Y^2 has the same significance as defined above)~~; and X^1 is cyclopropylene, or a salt thereof.

13. (Currently Amended) ~~The amine or the salt thereof~~ process according to claim 12, wherein R^1 is amino and R^{17} is a hydrogen atom.

14. (Currently Amended) ~~The amine or the salt thereof~~ process according to claim 13, wherein R^2 is carboxy.

Claims 15-22 (Cancelled).

23. (Currently Amended) ~~A~~ The method to inhibit proteasome comprising a process in which an effective amount of the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 is administered to a mammal including 1 to 9, wherein said compound is administered to a human.

24. (Currently Amended) ~~A~~ The method of inhibiting proteasome
accoding to claim 23, which is for treatment or prevention of a tumor comprising a step of
administering an effective amount of the carboxylic acid derivative or the pharmaceutically
acceptable salt thereof according to any one of claims 3 to 9 is administered to a mammal
including human.